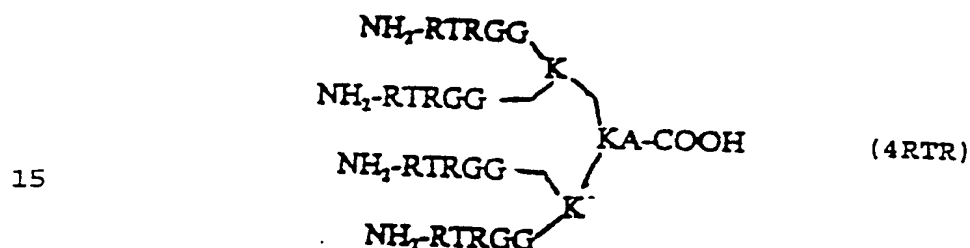


CLAIMS

5 1. A compound suitable for inhibiting the influx of polymorphonuclear leukocytes (PMNs) into a tissue involved in a chronic inflammatory disease in a mammal, which compound, in the presence of equimolar amounts of a) N-acetyl-Pro-Gly-Pro ("N-AcPGP"), b) a compound designated
10 as 4RTR with the formula I



which may form a complex with N-AcPGP, and c) the
20 compound, inhibits complex formation between N-AcPGP and 4RTR by at least 10% due to N-AcPGP being bound by the compound.

2. A compound according to claim 1, which compound produces at least a 25% inhibition of complex formation, preferably at least 50%, more preferably at least 70%, and most preferably at least 90%.

3. A compound according to claim 1 or 2, characterized in that the compound is a peptide.

4. A compound according to claim 1 or 2,
30 characterized in that the compound is a peptidomimetic.

5. A method of screening a number of compounds with respect to their capability to inhibit the formation of a complex between 4RTR and N-AcPGP, screening occurring by means of an assay comprising a competition reaction
35 between i) a compound A to be assayed and ii) a compound B capable of binding N-AcPGP having an equilibrium constant K of $5 \cdot 10^{-5} \text{ M}^{-1}$ or lower, compound A and compound B being in competition for the binding to a Pro-Gly-Pro (PGP) -

comprising compound C, with which the compound B is able to complex, having an equilibrium constant K of $5 \cdot 10^{-5} \text{ M}^{-1}$ or lower, and wherein a thus assayed compound A is selected having an equilibrium constant K for the reaction
5 between compound A and the PGP-comprising compound C of 10^{-4} M^{-1} or lower.

6. A method according to claim 5, characterized in that a compound A is selected having an equilibrium constant K of 10^{-5} M^{-1} or below, preferably 10^{-6} M^{-1} or below,
10 more preferably 10^{-7} M^{-1} or below, and most preferably 10^{-8} M^{-1} or below.

7. A method according to claim 5 or 6, characterized in that the compound C is N-R-Pro-Gly-Pro ("N-R-PGP"), wherein R is branched or linear alkyl- or
15 acyl group having 1 to 6 carbon atoms.

8. A method according to one of the claims 5 to 7, characterized in that the assay is a homogenous assay.

9. A method according to one of the claims 5 to 8, characterized in that the assay is based on fluorescence
20 (de)polarization or internal energy transfer.

10. A compound suitable for inhibiting the influx of PMNs in a tissue involved in a chronic inflammatory disease in a mammal, which compound E, in the presence of an equimolar amount of N-acetyl-Pro-Gly-Pro ("N-AcPGP"),
25 competes for binding to a PMN and inhibits the binding of N-AcPGP to the PMN by at least 10% as a result of N-AcPGP being bound by the compound, and which compound E does not induce activation of the PMN.

11. A compound according to claim 10, which
30 compound E inhibits binding by at least 25%, preferably by at least 50%, more preferably by at least 70% and most preferably by at least 90%.

12. A compound according to claim 10 or 11, characterized in that the compound is a peptide.

35 13. A compound according to claim 10 or 11, characterized in that the compound is a peptidomimetic.

14. A compound according to claim 10 or 11, characterized in that the compound is an antibody,

preferably a monoclonal antibody, and most preferably a human or humanized monoclonal antibody, or fragments thereof.

15 15. A method of screening a number of compounds with respect to their ability to inhibit the binding of N-AcPGP to a PMN, wherein screening occurs

a) by using an assay comprising a competition reaction between a compound E to be assayed and a compound D for the binding to a PMN, wherein compound D is capable
10 of competing with N-acetyl-Pro-Gly-Pro ("N-AcPGP") for binding to a PMN and at equimolar concentrations of the compound D and N-AcPGP, inhibits the binding of N-AcPGP by at least 50%, and at equimolar concentrations of the compound E and compound D, inhibits the binding of D to
15 the PMN by at least 10%, and

b) by contacting the compound E with a PMN and selecting a compound E which substantially does not induce activation of the PMN.

20 16. A method according to claim 15, characterized in that compound D is N-R-Pro-Gly-Pro, wherein R is a branched or linear alkyl or acyl group having 1 to 6 carbon atoms, preferably 1 to 2 carbon atoms, such as N-Ac-PGP or N-methyl-PGP.

25 17. A method according to claim 15 or 16, characterized in that the assay in respect to the activation of the PMN comprises measuring the polarization of the PMN.

30 18. A method according to claim 15 or 16, characterized in that the inhibition of the binding is established with the aid of flow cytometry.

19. An pharmaceutical composition comprising a compound according to one of the claims 1 to 4 or 10 to 14, or a compound selected with a method according to one of the claims 5 to 9 or 15 to 18, together with a
35 pharmaceutically acceptable carrier or excipient.

20. An application of a compound according to one of the claims 1 to 4 or 10 to 14, or a compound selected with a method according to one of the claims 5 to 9 or 15

to 18 for the preparation of the pharmaceutical composition suitable for the treatment of a chronic inflammatory disease in a mammal.

21. An application according to claim 20,
- 5 characterized in that the chronic inflammatory disease is a disease belonging to the group comprising chronic inflammatory bowel diseases, rheumatoid arthritis, and other auto-immune diseases, heart diseases that are characterized by an influx of neutrophilic granulocytes,
- 10 such as heart ischemia, Adult Respiratory Distress Syndrome (ARDS), asthma and lung emphysema.
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